DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

E. Edward Kavanaugh
President
Cosmetic, Toiletry, and
Fragrance Association
1101 17th Street, N.W., Ste. 300
Washington D.C. 20036-4702

OCT 1 1999

Re: Docket No. 78N-0038/CP11

Dear Mr. Kavanaugh:

On April 15, 1999, the Cosmetic, Toiletry, and Fragrance Association ("CTFA") submitted to the Food and Drug Administration ("FDA") a petition under sections 10.30 and 10.35 (21 CFR 10.30 and 10.35) requesting that the Commissioner of Food and Drugs (1) stay the effective date of the agency's final rule requiring a standard format for all over-the-counter ("OTC") drug products as it applies to sunscreen drug products and (2) stay or refrain from publishing a "partial" final OTC monograph for sunscreen drug products. The petition also requested under sections 10.25 and 10.30 (21 CFR 10.25 and 10.30) that the agency initiate an administrative process to publish a "comprehensive" monograph for OTC sunscreen drug products.

CTFA submitted the petition just prior to the expiration of a congressional mandate directing FDA to publish regulations for OTC sunscreen products. See Section 129 of the FDA Modernization Act of 1997 (Pub. L. 105-115) ("FDAMA") (requiring FDA to issue final regulations not later than May 1999).

The primary basis for CTFA's petition was the concern that the agency, in an effort to meet the FDAMA deadline, would only be able to publish a final monograph for sunscreens intended to protect against ultraviolet B ("UVB") radiation. Because of the health concerns associated with ultraviolet A ("UVA") radiation, CTFA suggested that the agency forego the FDAMA deadline, rather than publish a "UVB-only" monograph.

CTFA also took the position that the agency's recently issued general labeling rule regarding the format and content of OTC drug products (21 CFR 201.66) is "inadequate"

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when applied to sunscreen drug products and may force manufacturers to remove sunscreen ingredients from their products.

On May 21, 1999, after giving preliminary consideration to CTFA's petition, the agency issued its final monograph within the time frame required by Congress. The agency, however, has continued to consider the issues raised by CTFA in its petition. Having carefully considered the petition, the information submitted in support of the petition, and all other relevant information, the agency has decided to grant the petition in part and deny the petition in part.

I. Background

Sunscreen drug products generally are intended to help prevent certain harmful effects of the sun. In May 1993, the agency published a notice of proposed rulemaking or "tentative final monograph (TFM)" for OTC sunscreen drug products (58 FR 28194, May 12, 1993). The TFM proposed the conditions under which sunscreen products would be considered generally recognized as safe and effective, under section 201(p) of the Federal Food, Drug, and Cosmetic Act (the "Act"), and not misbranded under section 502 of the Act.

The TFM proposed labeling for products that claim to protect against UVB radiation and discussed the types of labeling claims that could be used with products that contain UVA-absorbing ingredients (see 58 FR at 28233). The TFM also included a list of proposed sunscreen active ingredients (see 58 FR at 28295), including ingredients that were believed to have absorption spectra extending into the UVA range (see 58 FR at 28233). As discussed in the TFM, both UVB and UVA radiation are associated with adverse health effects:

> The agency is aware that UVA radiation contributes to both acute and chronic skin damage such as erythema, melanogenesis, carcinogenesis, drug-induced photosensitivity, photoaging, and morphological alterations of Langerhans cells. Although UVB radiation is much more erythemogenic than UVA radiation, the large amount of UVA radiation present in the solar spectrum at the earth's surface results in a significant contribution to erythemogenesis. . . . It has also been reported that UVA radiation penetrates the skin more efficiently than UVB. Approximately 40 to 50 percent of UVA radiation is transmitted through Caucasian epidermis compared to 10 to 30 percent of UVB radiation. UVA radiation penetrates more deeply into the dermis than does UVB radiation. In addition, the agency is concerned that sunscreens with higher SPF values allow consumers to remain in the sun for long periods of time without burning, thus increasing UVA exposure. Accordingly, protection against UVA radiation is much more important than previously realized. The agency believes that protection against UVA radiation may be as important to consumers' well-being as protection against UVB radiation.

58 FR at 28233 (references omitted)

The TFM also proposed a set of testing procedures for measuring a product's "Sun Protection Factor (SPF)." The SPF value is a well accepted measure of the performance of sunscreens that absorb erythema-causing UV radiation. It does not, however, fully describe the performance of a product with respect to UVA protection. As the agency acknowledged in the TFM, "currently there is no generally acceptable method for determining a meaningful UVA protection factor that is analogous to the SPF" (58 FR at 28249).[1]

Following publication of the TFM, the agency has continued to work closely with the sunscreen industry, including representatives of CTFA, to develop standardized UVA testing procedures and an accurate, helpful way to present information about UVA performance in labeling. On April 5, 1994, the agency announced a public meeting to discuss UVA testing procedures and reopened the administrative record to allow additional submissions on UVA-related issues (59 FR 16042). Within the past three years, the agency has amended the TFM to add UVA-absorbing sunscreen ingredients to the proposed list of monograph ingredients (see 61 FR 48645, Sept. 16, 1996 (amending the TFM to include avobenzone); 63 FR 56584, Oct. 22, 1998 (amending the TFM to include zinc oxide)). The agency also amended the TFM to include proposed indications for these two UVA-absorbing ingredients, such as "provides broad spectrum protection" and "provides protection from the UVA rays that may contribute to skin damage and premature aging of the skin" (see 61 FR at 48655; 63 FR at 56589).

On November 21, 1997, Congress enacted the Food and Drug Administration Modernization Act of 1997 or "FDAMA". Included within FDAMA was section 129, which provided as follows:

> Not later than 18 months after the date of enactment of this Act, the Secretary of Health and Human Services shall issue regulations for over-the-counter sunscreen products for the prevention or treatment of sunburn.

Section 129 prompted FDA to identify those parts of the monograph which could be finalized within the time frame set by FDAMA. In late 1997, FDA was still working with the industry to develop labeling and testing standards for UVA radiation. As recently as January 27, 1999, the agency held a public meeting to continue work on developing UVA testing methods and labeling (see Docket No. 78-0038, Rpt. 9). Given these outstanding issues, the agency decided to address the FDAMA deadline by finalizing the UVB portions of the TFM (and related provisions on water resistant test methods and cosmetic labeling).

On May 21, 1999, FDA published in the Federal Register a final OTC monograph for sunscreen products. The monograph included a list of 16 active ingredients and required labeling for products that contain one or more of these ingredients. Also included was a

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[1]Prior to issuing the TFM, the agency announced a series of public meetings to discuss UVA testing and labeling and to gather additional information in support of setting monograph standards for OTC sunscreen products (see, e.g., 50 FR 41958, Oct. 16, 1985; 51 FR 45060, Dec. 16, 1986; 52 FR 5342, Feb. 20, 1987).

standardized test for measuring SPF values[2] and standard methods for measuring the water resistant properties of sunscreens. Last, the monograph included modifications to the agency's general OTC drug labeling rule (21 CFR 201.66) to accommodate certain sunscreen products that are packaged in small containers, are intended to be applied to limited areas of the face, and otherwise meet the factors discussed in the OTC labeling rule for monograph-specific modifications (see 64 FR at 27681-82; 64 FR at 13270).

The monograph did not, however, address active ingredients, labeling, and test methods for products intended to provide UVA coverage. As the agency stated in the May 21, 1999, notice:

> This final monograph completes the TFM except for certain testing issues and UVA labeling, which the agency will discuss in future issues of the Federal Register. Until then, UVA labeling may continue in accord with the TFM and its amendments.

64 FR at 27666-67.

The agency set a two-year effective date for the OTC monograph (21 CFR part 352) and the related "negative monograph" (21 CFR § 310.545) (see 64 FR 27666). The agency also set a two-year effective date for part 700 (21 CFR § 700.35), which addresses products that contain a sunscreen active ingredient for a non-sunscreen (i.e., non-therapeutic, non-physiologic) use. The agency set a one-year effective date for part 740 (21 CFR § 740.19) based on a finding of a significant safety issue (see 64 FR at 27686). Section 740.19 requires a warning statement on cosmetic products that are intended for use as "suntanning preparations" but do not contain a sunscreen active ingredient.

Following issuance of the final monograph, FDA's Division of OTC Drug Products issued a "feedback" letter to CTFA on a proposed protocol for testing the relative degree of UVA protection of sunscreen drug products. See July 16, 1999, letter from Dr. Charles Ganley, Director, Div. of OTC Drug Products, to Thomas Donegan, Jr., Vice President and Legal Counsel, CTFA. On July 22, 1999, the agency held a public meeting to discuss the testing and labeling of sunscreen products with SPF values above 30. At that meeting, CTFA requested that the agency defer implementation of the monograph, to allow for the completion of the UVA portions of the TFM. In September 1999, representatives of CTFA met with the agency and requested an extension of time, to December 2002, to work with the agency to resolve outstanding UVA and UVB testing and labeling issues. CTFA stated that it is

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[2]As discussed in the May 21, 1999, Federal Register notice, the SPF test method in the final monograph has been shown to be accurate and reproducible when measuring SPF values up to 30. The final monograph method has not been shown to provide accurate and consistent SPF values when used by different laboratories to test products formulated to provide protection higher than SPF 30. See 64 FR at 27680; see also Sept. 2, 1999, "feedback" letter from the Division of OTC Drug Products to CTFA at 1. The agency, however, has specifically invited interested persons to continue developing test methods for measuring SPF values higher than 30, and to submit data to the agency in support of such methods. See 64 FR at 27675.

prepared to work expeditiously with the agency and that it believes a comprehensive "UVA-UVB" monograph can be completed in advance of December 2002.

II. Response

Approximately one month before the FDAMA deadline, CTFA submitted this petition requesting that the agency refrain from publishing a final OTC sunscreen monograph that related only to the formulation, testing, and labeling of sunscreen drug products for protection against UVB radiation.

CTFA stated that recent medical evidence makes clear that UVA protection "may be the most important factor in preventing skin cancer caused by sun exposure," and that the most important long-term benefits associated with the use of sunscreens – preventing skin cancer and premature aging, according to the petition – are based on the filtering of UVA radiation. A final monograph that lacked testing and labeling standards for UVA filtration would not, according to the petition, be consistent with the public interest (Petition or "Pet." at 4, 6).

The petition also argued that a "partial" final monograph would cause disruption within the industry, and confusion for consumers, if manufacturers were required to label products several times – to conform to the final monograph, to the new OTC labeling rule, and to UVA parts of the monograph as they are finalized (Pet. at 12).

Last, the petition suggested that FDA would "more fully support Congressional intent" by waiting until it could publish a "comprehensive" monograph, rather than publishing a "partial" monograph by the May 1999 FDAMA deadline. According to CTFA, section 129 was only intended to "encourage" the agency to work toward completing the monograph. The sponsors of section 129 did not intend to require FDA to issue a "partial", "UVB-only" monograph by the FDAMA deadline (Pet. at 11).

For the reasons stated below, the part of the petition asking the agency to refrain from publishing an OTC sunscreen final monograph is moot (and therefore is denied). However, the part of the petition asking the agency to establish a process for the development of a comprehensive monograph that includes standards for UVA and UVB protection and any appropriate further modifications to the general OTC labeling rule to accommodate certain sunscreen products, is granted.

To implement this response, the agency will publish in the Federal Register an amendment to the "Effective Dates" section of the May 21, 1999, Federal Register document. The agency will extend, until December 31, 2002, the effective dates for parts 310, 352, and

700 of the final rule.[3] This amended effective date is intended to provide the agency, with input from all interested persons (including CTFA), the opportunity to complete work on a comprehensive monograph with a projected effective date of December 31, 2002.

A. Request that FDA Refrain from Issuing a "Partial" Monograph

The agency disagrees with the argument that it could have satisfied the directive in FDAMA by delaying publication of a final rule indefinitely, until the agency was in a position to publish a comprehensive monograph. The agency also disagrees with the argument that Congress specifically intended for FDA not to issue a "partial monograph."

Section 129 states that "[n]ot later than 18 months after the date of enactment of [FDAMA]," the Secretary or, by delegation, FDA "shall issue regulations for over-the-counter sunscreen products for the prevention or treatment of sunburn" (emphasis added).[4] Moreover, the Joint Statement accompanying section 129 states that the intent of the provision is to require FDA "to issue regulations within 18 months." The conferees also appear to have anticipated the idea that FDA would be required to publish a partial monograph: "The conferees recognize that various technical and scientific issues may take longer to resolve than other aspects of the rulemaking. The conferees do not intend that all regulation in this area be complete or comprehensive by a specified date."

Based on the plain language of section 129, FDA denies your petition (which has now been rendered moot) to refrain from publishing a final monograph, and denies your request for an indefinite stay.

B. Request for a Process to Allow for Issuance of a Comprehensive Monograph

The agency agrees with CTFA that "the public health will be best served by sunscreen products that will protect the public from harmful exposure to both UVA and UVB radiation" (Pet. at 15). As discussed above, the agency recognized the public health significance of UVA radiation in the TFM (see 58 FR 28194 at 28232-33, 28248-50), in subsequent amendments to the TFM (61 FR 48645, Sept. 16, 1996; 63 FR 56584, Oct. 22, 1998), and in public

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[3]This response does not affect the one-year effective date for 21 CFR 740.19. Section 740.19 addresses cosmetic products that are used in tanning but do not provide protection from UV radiation. Section 740.19 requires the addition of a single warning statement on such products. These products are not subject to the monograph. Moreover, the primary argument in favor of the petition - to obtain comprehensive UVA and UVB labeling for products intended to protect against the sun - is unrelated to section 740.19. Because of the health concerns associated with such products (see 58 FR at 28207), the agency assigned a separate, earlier effective date for this provision (see 64 FR at 27669, 27686).

[4]The use of the phrase "prevention or treatment of sunburn" suggests that Congress, at a minimum, was directing the agency to complete its sunscreen regulations for UVB coverage by May 1999. While the action spectra for the different types of skin damage caused by sun exposure have not been precisely characterized, UVB radiation (together with shorter-wavelength UVA radiation) is commonly associated with sunburn, while UVA radiation is commonly associated with photoaging of the skin and skin cancer. See, e.g., Pet. at 16-21.

meetings held both before and after publication of the TFM (see, e.g., 59 FR 16042, April 5, 1994).

The agency also agrees that it is important to minimize the potential for incremental, repeated relabeling of sunscreen drug products. Indeed, the agency carefully considered this point when it issued the May 21, 1999, final monograph. FDA selected a two-year effective date for the monograph to allow manufacturers to coordinate the sunscreen changes with labeling changes required under the general OTC labeling rule.[5] Also, as the agency noted in the "Analysis of Impacts" in the May 1999 final rule, FDA estimates that 90 percent of the sunscreen industry redesigns and relabels their products every two years (64 FR at 27684). Thus, a two-year effective date would allow most firms to coordinate the changes required by the monograph, and by the general labeling rule, within the typical redesign cycle.

When it issued the rule in May 1999, FDA's expectation was that a comprehensive sunscreen monograph was more than two years away from publication. Given that prediction, the agency decided to require implementation of the monograph in two years, rather than wait for completion of a more comprehensive rule.

CTFA, however, is proposing that a comprehensive monograph can be completed in time for a December 2002 target effective date. In the petition and in recent public meetings, CTFA has stated its intent to work expeditiously on behalf of its members toward a comprehensive final monograph. In light of CTFA's proposal that an extension through the end of 2002 will be sufficient for it to submit the data needed to complete the monograph, the agency has reconsidered its decision with respect to implementation of the final rule.

The agency recognizes that a comprehensive relabeling of sunscreen products – if it can be achieved expeditiously – may help minimize consumer confusion and thus may be preferable to the successive introduction of "UVB" and "UVA" labeling. Also, a comprehensive approach will give the agency the opportunity to consider ways to integrate UVA and UVB labeling and to address outstanding technical issues on UVA and high SPF test methods. The agency agrees that if integrated, broad spectrum labeling can be finalized in advance of December 2002, the incremental benefits of having consumers become familiar sooner with the "UVB" labeling in the May 1999 rule may be outweighed by the benefits of achieving a single, comprehensive labeling change.

In short, FDA is granting the petition by extending the effective date of the monograph to December 31, 2002, with the expectation that a comprehensive UVA-UVB monograph can be issued in advance of that date.

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[5]Under the implementation plan set forth in the general labeling rule, OTC drug products that are not the subject of a final monograph as of May 2001 must comply with the new labeling requirements at the time of their next major labeling revision (64 FR 13724). FDA set a May 2001 effective date for the sunscreen monograph to allow firms to come into compliance with both rules at the same time.

C. Request for a Stay of the General Labeling Rule

On March 17, 1999, the agency issued a general labeling rule applicable to all OTC drug products (21 CFR § 201.66). The rule establishes standardized format and content requirements to help consumers read and understand OTC drug labeling, and to aid in comparing and selecting OTC drug products. See 64 FR 13254 (Mar. 17, 1999). For products that become the subject of a final monograph after the effective date of the general labeling rule (i.e., May 17, 1999), compliance with the labeling rule is required as of the effective date of the applicable final monograph. See 64 FR at 13274.

You have asked the agency to stay implementation of the general OTC labeling rule, as it applies to sunscreen products, "until such time as FDA promulgates a comprehensive Final Monograph for OTC sunscreen drug products" (Pet. at 2).

As a result of the amendment to the effective date, sunscreen products are not required to comply with the general OTC labeling rule until December 31, 2002. The amended effective date thus will allow the agency to consider CTFA's general and specific concerns regarding the application of the new labeling format to sunscreen drug products.

As the agency stated in its general OTC labeling rule:

> In some cases (e.g., lipsticks or lip balms containing sunscreen), minimal information is needed for the safe and effective use of the product. Such products may typically be packaged in small amounts, have a high therapeutic index, carry extremely low risk in actual consumer use situations, provide a favorable public health benefit, require no specified dosage limitation, and require few specific warnings and no general warnings (e.g., pregnancy or overdose warnings). The agency will identify products with these characteristics and will consider appropriate exemptions in their respective monographs and drug marketing applications to the extent possible. In addition, under new §201.66(e), FDA, on its own initiative, or in response to a written request from any manufacturer, packer, or distributer, may exempt or defer one or more specific requirements set forth in §201.66 (a) through (d).

64 FR at 13270 (emphasis added)

In the May 1999 final monograph, the agency identified several modifications to the general labeling requirements, to facilitate the use of the new labeling format on certain categories of sunscreen products (see 64 FR at 27681-82, 27689). The agency will continue to consider appropriate modifications as it works toward a comprehensive, final sunscreen monograph. In short, through this action the agency believes it is providing the relief you were seeking.

III. Conclusion

The agency is granting the petition to allow for the expeditious completion of a revised final monograph that will establish standards for UVA formulation ingredients, labeling, and testing. The process for completing the revised final monograph will also allow the agency to resolve issues associated with the testing and labeling of high SPF values (i.e., values above SPF 30), and consider ways to integrate UVA and UVB indications for use and performance statements. The agency will also continue to consider appropriate modifications to the general OTC labeling rule, to accommodate this category of products.

The agency will implement this petition response by publishing a notice in the Federal Register amending the effective date of the May 1999 final monograph, and by outlining in that notice the process that will be followed for the expeditious completion of a comprehensive UVA-UVB monograph.

Sincerely yours,

for Dennis E. Baker
Associate Commissioner
for Regulatory Affairs

M E M O R A N D U M

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE:

FROM: Director
Division of OTC Drug Products, HFD-560

SUBJECT: Material for Docket No. 78N-0038 /CP11

TO: Dockets Management Branch, HFA-305

[X] The attached material should be placed on public display under the above referenced Docket No.

[ ] This material should be cross-referenced to Comment No. _____

Charles J. Ganley, M.D.

Attachment

HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

CROSS REFERENCE SHEET

Docket Number/Item Code:	78N-0038/PAV2
See Docket Number/Item Code:	98N-0337/PAV1 96N-0420/PAV1 90P-0201/PAV2 95N-0259/PAV1